Emtricitabine

Brand Name: Emtriva

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Drug Description

Emtricitabine, also referred to as FTC, is a nucleoside reverse transcriptase inhibitor (NRTI). Emtricitabine is the (-) enantiomer of a thio analogue of cytidine; it differs from other cytidine analogues by a fluorine in the 5 position. [1]

HIV/AIDS-Related Uses

Emtricitabine was approved by the FDA on July 2, 2003 for use in combination with other antiretroviral agents for the treatment of HIV infection in adults age 18 and older. Safety and effectiveness in pediatric patients have not been established. In antiretroviral treatment experienced patients, the use of emtricitabine may be considered for adults with HIV that is expected to be susceptible to emtricitabine as assessed by genotypic or phenotypic testing.[2]

Non-HIV/AIDS-Related Uses

Emtricitabine is being studied for the treatment of chronic hepatitis B virus (HBV) infection.[3]

Pharmacology

Emtricitabine, a synthetic nucleoside analogue of cytosine, undergoes phosphorylation by means of cellular enzymes. The product of phosphorylation, emtricitabine 5'-triphosphate, inhibits viral DNA synthesis by competing with the natural substrate deoxycytidine 5'-triphosphate for incorporation into viral DNA and terminating the DNA chain at the point of incorporation.[4]

Emtricitabine is rapidly and extensively absorbed following oral administration, reaching peak plasma concentrations (Cmax) at 1 to 2 hours post-dose. In one clinical trial, the mean absolute bioavailability of emtricitabine was 93% following multiple doses of the drug. The mean steady state Cmax was 1.8 plus or minus 0.7 mcg/ml and the area under the plasma concentration-time curve (AUC) over a 24-hour dosing interval was 10.0 plus or minus 3.1 hr mcg/ml. The mean steady state plasma trough concentration 24 hours after an oral dose was 0.09 mcg/ml.[5]

Emtricitabine is in FDA Pregnancy Category B. Animal studies revealed no increased incidences of fetal variations or malformations in mice and rabbits at 60- and 120-fold higher exposures, respectively, than the human exposure at the recommended daily dose. However, there have been no adequate well-controlled studies in pregnant women. Results of animal studies are not always predictive of human response and emtricitabine should be used during pregnancy only if clearly needed. It is not known whether emtricitabine is distributed into human milk.[6]

Emtricitabine is less than 4% bound to plasma proteins and protein binding is independent of drug concentration over a range of 0.02 to 200 mcg/ml. In vitro studies indicate that emtricitabine does not inhibit CYP450 enzymes. Following administration of 14C-emtricitabine, the dose was 86% recovered in urine and 14% in feces. Thirteen percent was recovered in urine as metabolites, including 3'-sulfoxide diastereomers and 2'O-glucuronide; no other metabolites were identifiable. The plasma half-life of emtricitabine is approximately 10 hours. Renal clearance of the drug exceeds estimated creatinine clearance, indicating elimination by glomerular filtration and tubular secretion. In patients with renal impairment, Cmax and AUC were increased.[7]

HIV isolates with reduced susceptibility to emtricitabine have been recovered from some patients treated with emtricitabine alone or in combination with other antiretroviral agents. Viral isolates from 37.5% of patients with virologic failure had reduced susceptibility to emtricitabine. Genotypic analysis revealed the cause as M184V/I mutations in the HIV reverse transcriptase gene. Cross-resistance has been noted among some nucleoside analogues. Emtricitabine-resistant isolates were cross-resistant to lamivudine and zalcitabine but retained susceptibility to abacavir, didanosine, stavudine, tenofovir, and zidovudine, as well as to the nonnucleoside reverse transcriptase inhibitors delavirdine, efavirenz, and nevirapine.[8]

Adverse Events/Toxicity

The most frequently reported adverse effects of

Emtricitabine

Adverse Events/Toxicity (cont.)

emtricitabine are headache, nausea, skin rash, and skin discoloration on palms and soles.[9]

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogues alone or in combination, including emtricitabine. In some patients coinfected with HIV and hepatitis, exacerbation of hepatitis B has been reported after discontinuing treatment with emtricitabine.[10]

Redistribution of body fat, peripheral wasting, facial wasting, breast enlargement, and cushingoid appearance have been observed in patients receiving antiretroviral therapy.[11]

Drug and Food Interactions

Emtricitabine may be administered with or without food: the AUC was unchanged and Cmax decreased by 29% when the drug was administered with a 1,000-calorie, high-fat meal.[12]

Emtricitabine has been evaluated in healthy volunteers in combination with tenofovir disoproxil fumarate (tenofovir DF), indinavir, famciclovir, and stavudine. Results showed no interactions except for a small increase in plasma trough concentrations of emtricitabine when it is administered concurrently with tenofovir DF.[13] Because elimination of emtricitabine is probably via both glomerular filtration and active tubular secretion, there may be competition for elimination with other compounds that are also renally eliminated.[14]

Contraindications

Emtricitabine is contraindicated in patients with previously demonstrated hypersensitivity to any of the components of the drug product.[15]

Clinical Trials

For information on clinical trials that involve Emtricitabine, visit the ClinicalTrials.gov web site at http://www.clinicaltrials.gov. In the Search box, enter: Emtricitabine AND HIV Infections.

Dosing Information

Mode of Delivery: Oral.[16]

Dosage Form: Capsules containing 200 mg of emtricitabine.[17]

The recommended dose of emtricitabine for adults 18 years of age and older is 200 mg once daily. The dosing interval of emtricitabine should be adjusted in patients with baseline creatinine clearance less than 50 ml/min. The dosing interval recommendations are: creatinine clearance 30 to 49 ml/min, 200 mg every 48 hours; creatinine clearance 15 to 29 ml/min, 200 mg every 72 hours; and creatinine clearance less than 15 ml/min, 200 mg every 96 hours.[18]

Storage: Store at 25 C (77 F); excursions permitted to 15 C to 30 C (59 C to 86 F).[19]

Chemistry

CAS Name: (2R-cis)-4-Amino-5-fluoro-1-[2-(hydroxymethyl)-1,3-oxathiolan-5-yl]-2(1H)-pyrimidinone[20]

CAS Number: 143491-57-0[21]

Molecular formula: C8-H10-F-N3-O3-S[22]

C 38.86%, H 4.08%, F 7.68%, N 17.00%, O 19.41%, S 12.97%[23]

Molecular weight: 247.25[24]

Melting point: 136 to 140 C[25]

Physical Description: White to off-white powder.[26]

Solubility: Approximately 112 mg/ml in water at 25 C (77 F).[27]

Other Names

2'-Deoxy-5-fluoro-3'-thiacytidine[28]

2-FTC[29]

524W91[30]

Emtricitabine

Other Names (cont.)

BW524W91[31]

dOTFC[32]

FTC[33]

Coviracil[34]

BW 1592[35]

Emtricitabina[36]

5-fluoro-1-[(2R,5S)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]cytosine[37]

Further Reading

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For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

• Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET

• Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

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